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(54) Title: NEUROPROTECTIVE ACTIVITY OF ACTIVATED PROTEIN C IS INDEPENDENT OF ITS ANTICOAGULANT ACTIVITY

(57) Abstract: Activated protein C (APC), prodrug, and/or a variant thereof may be used as an inhibitor of apoptosis or cell death and/or a cell survival factor, especially for stressed or injured cells or tissues of the nervous system including subjects with neurodegenerative disorders. Novel biological functions (e.g., neuroprotection) can be independent or separated from inhibition of clotting or inflammation, and other biological properties of APC (e.g., antithrombotic activity, ability to reduce NFkB-regulated gene expression). It can be used in the treatment of disease or other pathological conditions by at least inhibiting the p53-dependent and/or caspase-3-dependent pro-apoptotic signaling pathways in stressed or injured cells. Thus, APC, prodrugs, and variants thereof (e.g., APC protease domain mutants with reduced anti-coagulant activity) are prototypes of a class of agents for preventing apoptosis or cell death and/or promoting cell survival by direct action on brain cells. New protein C and/or APC variants with reduced anticoagulant activity may be selected thereby.